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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/611,399 | 07/01/2003 | John R. Desjarlais | A-71273-3/RMS/RMK<br>463077- | 1891 |

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| EXAMINER | |
|---|---|
| EMCH, GREGORY S | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1649 | |

DATE MAILED: 12/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/611,399 | DESJARLAIS ET AL. | |
| | Examiner | Art Unit | |
| | Gregory S. Emch | 1649 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *01 July 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-44* are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Election/Restrictions*

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-16, 34, and 35 drawn to a method of antagonizing a naturally occurring TNFSF protein, classified in class 435, subclass 7.1.

II. Claims 17-26, 33, and 36-44 drawn to a variant TNFSF monomer protein, oligomers comprising said protein, and pharmaceutical compositions of said protein, classified in class 530, subclass 350, for example.

III. Claims 27-32, drawn to a nucleic acid encoding a variant TNFSF monomer protein, vectors, host cells, methods of recombinantly producing a variant TNSF, classified in class 536, subclass 23.5 and class 435, subclasses 320.1, 252.3, and 69.1, for example.

The inventions are distinct, each from the other because of the following reasons:

Invention II is related to Inventions I and as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the variant TNFSF monomer protein can be used in a method of antagonizing a naturally occurring TNFSF protein, or a method of treatment of a TNFSF disorder by administering a

variant TNFSF protein, but can also be used in a method of generating antibodies to the variant TNFSF protein, which is a materially different method.

Invention III is unrelated to Inventions I. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the nucleic acids, host cells, and method of recombinantly producing the protein are not used in the method of antagonizing a naturally occurring TNFSF with a variant TNFSF protein and are not used in a method of treatment comprising administering a variant TNFSF protein.

Inventions II and III are independent and distinct, each from each other, because they are products which possess characteristic differences in structure and function and each has an independent utility that is distinct for each invention which cannot be exchanged. The polynucleotide of Group III and the polypeptide of Group II are patentably distinct for the following reasons: polypeptides (composed of amino acids) and polynucleotides (composed of purines and pyrimidines) are structurally distinct molecules; any relationship between them depends upon the information provided by the nucleic acid sequence open reading frame as it corresponds to the primary amino acid sequence of the encoded polypeptide. Furthermore, the search of the inventions of Group III and II together would impose a serious search burden. The two inventions have a separate status in the art as shown by their different classifications. In cases such as this where descriptive sequence information is provided, the protein and nucleic acid sequences are searched in databases that are not coextensive. In addition, the

technical literature search is not coextensive. A protein may be described in the literature prior to the concomitant isolation and expression of the nucleic acid sequence. Similarly, there may be "classical" genetics papers that describe the gene but not the polypeptide.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, separate search requirements and/or divergent subject matter, restriction for examination purposes as indicated is proper.

**Rejoinder under Ochiai/Brouwer**

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312. In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable,

the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. § 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

***Election of species***

I) In addition to the above restriction requirement, a further election of species is required as follows:

Claims 1-44 are generic to a plurality of disclosed patentably distinct species of TNFSF proteins comprising TNF-$\alpha$, lymphotoxin-$\alpha$, lymphotoxin-$\beta$, Fas ligand (FasL),

TRAIL, CD40 ligand (CD40L), CD30 ligand, CD27 ligand, Ox40 ligand, APRL, BLys, 4-IBBL, TRANCE, or RNALK (OPGL) (see pg 4, lines 4-7 of the specification). Applicant is required under 35 U.S.C. 121 to elect a single disclosed species of TNFSF protein, even though this requirement is traversed.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

II) In addition to the above restriction requirement and species election, a further election of species is required as follows:

A) Applicant must elect one of the following patentably distinct species of position in the Large Domain in the claimed invention: 28, 29, 30, 31, 32, 33, 34, 63, 64, 65, 66, 68, 69, 77, 112, 113, 114, 115, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, and 147.

B) Applicant must elect one of the following patentably distinct species of position in the Small Domain in the claimed invention: 72, 73, 74, 75, 76, 78, 79, 95, 96, 97, and 98.

C) Applicant must elect one of the following patentably distinct species of position in the DE Loop in the claimed invention: 84, 85, 86, 87, 88, and 89.

D) Applicant must elect one of the following patentably distinct species of position in the Trimer Interface in the claimed invention: 11, 13, 15, 34, 36, 53, 54, 55, 57, 59, 61, 63, 72, 73, 75, 77, 87, 91, 92, 93, 94, 95, 96, 97, 98, 99, 102, 103, 104, 109, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 147, 148, 149, 151, 155, 156, and 157.

Each position is considered to constitute a patentably distinct species because an amino acid change at that position produces a protein with a different structure, and requires a separate search. Search of more than a single species would constitute an undue burden on the Office.

Applicant is required under 35 U.S.C 121 to elect one of each of the following species: a) a single position in the Large Domain; b) a single position in the Small Domain; and c) a single position in the DE Loop; and d) a single position in the Trimer Interface loop for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 1-44 are generic.

III) In addition to the above restriction requirement and species elections, a further election of species is required as follows:

Applicant must elect one of the following species of domain modifications or combinations of domain modifications:

1) Large Domain and Small Domain (with or without Trimer Interface);

2) Large Domain and DE Loop (with or without Trimer Interface);

3) Small Domain and DE Loop (with or without Trimer Interface);

4) Large Domain, Small Domain, and DE Loop (with or without Trimer Interface);

5) Trimer Interface and Large Domain;

6) Trimer Interface and Small Domain;

7) Trimer Interface and DE Loop ;

8) Large Domain;

9) Small Domain;

10) DE Loop ; or

11) Trimer Interface;

Each species of domain modification or combination of domain modifications is considered to constitute a patentably distinct species because each modification ro combination of modifications produces a protein with a different structure, and requires a separate search. Search of more than a single species would constitute an undue burden on the Office.

Applicant is required under 35 U.S.C 121 to elect a single domain modification or combination of domain modifications for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 1-44.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim

is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C 103(a) of the other invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1649.

***Advisory Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory S. Emch whose telephone number is (571) 272-8149. The examiner can normally be reached on Monday through Friday from 8:30AM to 5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres can be reached at (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gregory S. Emch, Ph. D.
Patent Examiner
Art Unit 1649
December 23, 2005

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER